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JENKINS & WILSON, PA
3100 TOWER BLVD
SUITE 1400
DURHAM, NC 27707

EXAMINER

SEHARASEYON, JEGATHEESAN //

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| ART UNIT | PAPER NUMBER |
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1647

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/856,836

Applicant(s)

DATTA ET AL.

Examiner

Jegatheesan Seharaseyon

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-67 and 75-80 is/are pending in the application.
- 4a) Of the above claim(s) 1-13, 30-67 and 75-77 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-29 and 78-80 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Claims 68-74 have been cancelled. Claims 1-67 and 75-80 are pending.
2. Applicant's election of Group III, claims 14-29 and newly added claims 78-80, drawn to nucleic acid encoding a protein, a vector and a host cell in Paper No. 10 (1/2/03) is acknowledged. In addition, Applicant has elected SEQ ID NO: 1. Applicant did not distinctly and specifically point out any errors in the restriction requirement or traverse the restriction. Thus, the election has been treated as an election without traverse (MPEP§818.03(a)).

Claims 1-13, 30-67 and 75-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non elected group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10 (1/2/03). Therefore claims 14-29 and 78-80 are under consideration.

Oath/Declaration

3. The oath or declaration is defective. The oath or declaration is defective because: The Applicant claims priority to a provisional application in the specification. However, the oath and declaration only indicates the PCT application for priority. Appropriate correction is required. Providing an application data sheet can obviate this objection.

Specification

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

5. Claim 19 is objected to because of the following informalities: On line 2 of the claim 19 the word "is" needs to be inserted before "selected". Appropriate correction is required.

Drawings

4. The drawings have been objected to by the draftsman (see attached 948). Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16, 18-24, 26-28 and 78-80 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5a. Claims 14-16 and 29 are rejected as being vague and indefinite in the recitation of the term "STRAP polypeptide". Applicant should particularly point out and distinctly claim the STRAP by claiming structural or other identifying characteristics associated with the protein (e.g. amino acid sequence, molecular weight, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is. The specification gives no definition of what is intended by "STRAP", merely an example of one species. Therefore, the

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metes and bounds of the claim cannot be determined. Claims 20-24, 26-28 and 78-80 are rejected insofar as they depend on rejected claim 14.

5b. Claim 18 is indefinite because "further comprising" means 'in addition has'.

Therefore, it is not clear whether applicants intend, "comprising" or alternatively that the claimed nucleic acid has both the elements that are recited in claim 14 and that of claim 18.

5c. Claim 19 recites the limitation "The nucleic acid molecule of claim 18" in line 1.

However, claim 18 refers to a "nucleic acid segment" and not a molecule. There is insufficient antecedent basis for this limitation in the claim.

5d. Claim 19 is indefinite because the term "represented by" is not limiting, and even if it were, conditions are so vague that metes and bounds of what would hybridize cannot be determined.

5e. Claim 21 and 22 are indefinite because a "gene" is defined in the art as comprising a promoter. However, the claim recites that the gene is positioned under the control of a promoter. Therefore it is not clear what Applicants intend by "gene", nor how claim 21 is further limiting.

5f. Claims 78-80 are indefinite because the claims recite that the nucleic acid segment and the host cells comprise carriers. It is not clear whether Applicants intend a composition comprising the nucleic acid or host cells etc. and a carrier, or if not, exactly what is intended.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claims 14-16, 20-24, 26-29 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses STRAP polypeptide sequence of SEQ ID NO: 2 and the nucleotide encoding the STRAP polypeptide (SEQ ID NO: 1). This meets the written description and enablement provisions of 35 USC 112, first paragraph. However, the specification does not disclose all the STRAP polypeptide molecules that are capable of modulating TGF- β biological activity and the nucleotides encoding the same or the isolated or the isolated gene encoding STRAP polypeptide. The specification does not define what is meant by the generic term "STRAP" and discloses a single example. There is no description of what makes a STRAP polypeptide a STRAP, any STRAP from other species, or anything else that would be considered a "STRAP". In addition, there is no description of the isolated gene encoding the STRAP polypeptide. The claims as written, therefore, encompass polypeptide and nucleotide sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph. The specification does not provide written to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of STRAP polypeptide sequence of SEQ ID NO: 2 and the nucleotide encoding the STRAP polypeptide (SEQ ID NO: 1), the skilled artisan cannot envision all the detailed chemical structure of the claimed polypeptide and nucleotide sequences, regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the STRAP polypeptide sequence of SEQ ID NO: 2 and the nucleotide encoding the STRAP polypeptide (SEQ ID NO: 1 or degenerate variants thereof), but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed is not representative of the genus because the genus is unclear and potentially highly variant. As a result, it does not appear that the inventors were in possession of the scope of polypeptide sequences set forth in claims 14-16, 20-24, 26-29 and 78-80.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent

Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

6b. Claims 14-29 and 78-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the inhibition of TGF- β signaling does not reasonably provide enablement for modulating TGF- β biological activity. The term modulating would include both the inhibition and activation of TGF- β biological activity by any means. In addition, the specification while being enabling for STRAP polypeptide of SEQ ID NO: 2 does not provide enablement for all STRAP molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification as filed is insufficient to enable one skilled in the art to practice the claimed invention without an undue amount of experimentation. The inhibition of TGF- β signaling does not reasonably provide enablement for the scope of modulating TGF- β biological activity. Applicants have demonstrated that by using STRAP and Smad7 they are able to negatively regulate TGF- β signaling (Example 3 and 4, pages 77-79). However, it is unclear how and what other biological activity of TGF- β will be affected by STRAP polypeptide. In addition, there is no guidance provided for the mechanism of modulation of the biological activity either. While mechanism is not required, it can allow extrapolation of enablement to non-exemplified embodiments. Since applicant has not provided any working examples to indicate the modulation of the TGF- β biological activity either *in vitro* or *in vivo*, it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claims 14-29 and 78-80 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for modulating TGF- β biological activity.

In addition, claims 14-29 and 78-80 are rejected as single means claims in that they recite "STRAP polypeptide", but the specification only discloses proteins of SEQ ID NO: 2. MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be

nonenabling for the scope of the claim in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property (i.e. at least one biological property in common with STRAP), a fact situation comparable to *Hyatt* is present, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and the claims are not commensurate in scope with the specification.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6a. Claims 14-16, 19-24, 26-29 and 78-80 rejected under 35 U.S.C. 102(e) as being anticipated by Bandman et al. (U. S. Patent No: 5,834,240).

The present invention is directed to nucleic acid encoding STRAP polypeptide, which is a polypeptide that forms complexes with TGF- β and modulates its activity. Also claimed are expression vector, recombinant host cell and method making the polypeptide.

Bandman et al. teaches the human TGF- β associated protein (TGFAS). The nucleotide encoding the STRAP polypeptide of the instant invention has about 97% homology to SEQ ID NO: 2 of Bandman et al. reference (see Appendix A). This nucleic acid sequence of SEQ ID NO: 2, because of its high degree of homology is capable of hybridizing to SEQ ID NO: 1 of the instant invention. In addition, the reference also teaches the isolated gene under the control of promoters for expression in a variety of host/vector systems to produce the recombinant protein (column 11, line 34 to column 14, line 8). The reference further teaches the use of this invention along with pharmaceutically acceptable carriers for administration (column 19, line 13 to column 20 line 64). Therefore, the disclosure of Bandman et al. anticipates claims 14-16, 19-24, 26-29 and 78-80.

7. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

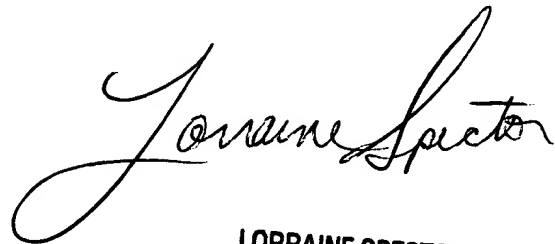
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JSS
March 6, 2003

A handwritten signature in cursive script, reading "Lorraine Spector". The signature is written in black ink and is positioned above the printed name and title.

**LORRAINE SPECTOR
PRIMARY EXAMINER**